

AMENDMENTS TO THE CLAIMS

Please cancel claims 63 and 66-93 without prejudice, as shown below.

Please amend claim 94 as shown in the following list of claims.

In compliance with 37 C.F.R. § 1.121, a complete listing of claims is presented below.

This listing of claims will replace all prior versions and listings of claims in this application.

1-63. (Canceled)

64. (Withdrawn) The pharmaceutical composition of Claim 64 which is a lyophilized powder.

65. (Withdrawn) The pharmaceutical composition of Claim 64 which is a solution.

66-93. (Canceled)

94. (Currently amended) The pharmaceutical composition of ~~Claim 86~~ comprising an ApoA-I agonist and a pharmaceutically acceptable carrier, excipient or diluent;

wherein the ApoA-I agonist is in the form of an ApoA-I agonist-lipid complex, said complex comprising an ApoA-I agonist and a lipid,

wherein the ApoA-I agonist comprises:

(i) a 22 to 29-residue peptide or peptide analogue which forms an amphipathic α -helix in the presence of lipids and which comprises formula (I):

$Z_1-X_1-X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-X_{12}-X_{13}-X_{14}-X_{15}-X_{16}-X_{17}-X_{18}-X_{19}-X_{20}-X_{21}-X_{22}-X_{23}-Z_2$

or a pharmaceutically acceptable salt thereof, wherein:

X_1 is Pro (P), Ala (A), Gly (G), Gln (Q), Asn (N), Asp (D) or D-Pro (p);

X_2 is an aliphatic residue;

X_3 is Leu (L) or Phe (F);

X_4 is an acidic residue;

X_5 is Leu (L) or Phe (F);

X_6 is Leu (L) or Phe (F);

X_7 is a hydrophilic residue;

X_8 is an acidic or a basic residue;

X_9 is Leu (L) or Gly (G);

X_{10} is Leu (L), Trp (W) or Gly (G);

X_{11} is a hydrophilic residue;

X_{12} is a hydrophilic residue;

X_{13} is Gly (G) or an aliphatic residue;

X_{14} is Leu (L), Trp (W), Gly (G) or Nal;

X₁₅ is a hydrophilic residue;

X₁₆ is a hydrophobic residue;

X₁₇ is a hydrophobic residue;

X₁₈ is Gln (Q), Asn (N) or a basic residue;

X₁₉ is Gln (Q), Asn (N) or a basic residue;

X₂₀ is a basic residue;

X₂₁ is an aliphatic residue;

X₂₂ is a basic residue;

X₂₃ is absent or a basic residue;

Z₁ is H₂N- or RC(O)NR'-;

Z₂ is -C(O)NRR, -C(O)OR or -C(O)OH or a salt thereof;

each R is independently -H, (C₁-C₆) alkyl, (C₁-C₆) alkenyl, (C₁-C₆) alkynyl, (C₅-C₂₀) aryl, (C₆-C₂₆) alkaryl, 5-20 membered heteroaryl or 6-26 membered alkheteroaryl or a 1 to 7-residue peptide or peptide analogue in which one or more bonds between residues 1-7 are independently a substituted amide, an isostere of an amide or an amide mimetic;

each R' is independently -H, (C₁-C₆) alkyl, (C₁-C₆) alkenyl, (C₁-C₆) alkynyl, (C₅-C₂₀) aryl, (C₆-C₂₆) alkaryl, 5-20 membered heteroaryl or 6-26 membered alkheteroaryl; and

each "—" between residues X₁ through X₂₃ independently designates an amide linkage, a substituted amide linkage, an isostere of an amide or an amide mimetic;

~~(ii) a 15 to 26 residue peptide or peptide analogue according to formula (I) which forms an amphipathic α -helix in the presence of lipids wherein one or two helical turns are deleted from formula (I), wherein a helical turn consists of 3 to 4 consecutive residues selected from residues X₁ to X₂₃ of formula (I);~~

~~(iii) a 22 to 29 residue altered peptide or peptide analogue according to formula (I) in which at least one of residues X₁, X₂, X₃, X₄, X₅, X₆, X₇, X₈, X₉, X₁₀, X₁₁, X₁₂, X₁₃, X₁₄, X₁₅, X₁₆, X₁₇, X₁₈, X₁₉, X₂₀, X₂₁, X₂₂ or X₂₃ is conservatively substituted with another residue; or~~

a N-terminally blocked form, a C-terminally blocked form, or an N- and C-terminally blocked form of formula (I).

95. (Previously presented) The pharmaceutical composition of Claim 94 wherein X₇ of the ApoA-I agonist is a basic residue.

96. (Previously presented) The pharmaceutical composition of Claim 94 wherein X₃, X₆, X₉ and X₁₀ of the ApoA-I agonist are hydrophobic residues.

97. (Previously presented) The pharmaceutical composition of Claim 94 wherein the ApoA-I agonist is a 22-23 residue peptide or peptide analogue according to formula (I).

98. (Previously presented) The pharmaceutical composition of Claim 97 comprising an ApoA-I agonist according to formula (I) wherein:

the “—” between residues X₁ through X₂₃ designates -C(O)NH-;

Z₁ is H₂N-; and

Z₂ is -C(O)OH or a salt thereof.

99. (Previously presented) The pharmaceutical composition of Claim 98 comprising an ApoA-I agonist according to formula (I) wherein:

X₁ is Pro (P), Ala (A), Gly (G), Asn (N), Gln (Q), Asp (D) or D-Pro (p);

X₂ is Ala (A), Val (V) or Leu (L);

X₃ is Leu (L) or Phe (F);

X₄ is Asp (D) or Glu (E);

X₅ is Leu (L) or Phe (F);

X₆ is Leu (L) or Phe (F);

X₇ is Lys (K), Arg (R) or Orn;

X₈ is Asp (D) or Glu (E);

X₉ is Leu (L) or Gly (G);

X₁₀ is Leu (L), Trp (W) or Gly (G);

X₁₁ is Asn (N) or Gln (Q);

X₁₂ is Glu (E) or Asp (D);

X₁₃ is Gly (G), Leu (L) or Aib;

X₁₄ is Leu (L), Nal, Trp (W) or Gly (G);

X₁₅ is Asp (D) or Glu (E);

X₁₆ is Ala (A), Nal, Trp (W), Leu (L), Phe (F) or Gly (G);

X₁₇ is Gly (G), Leu (L) or Nal;

X₁₈ is Gln (Q), Asn (N), Lys (K) or Orn;

X₁₉ is Gln (Q), Asn (N), Lys (K) or Orn;

X₂₀ is Lys (K) or Orn;

X₂₁ is Leu (L);

X₂₂ is Lys (K) or Orn; and X₂₃ is absent or Lys (K).

100. (Previously presented) The pharmaceutical composition of Claim 99 wherein X₂₃ of the ApoA-I agonist is absent.

101. (Previously presented) The pharmaceutical composition of Claim 94 comprising an ApoA-I agonist according to formula (I) wherein one of X₁₈ or X₁₉ is Gln (Q) or Asn (N) and the other of X₁₈ or X₁₉ is Lys (K) or Orn.

102. (Withdrawn) The pharmaceutical composition of Claim 94 comprising an ApoA-I agonist according to formula (I) wherein each of X₉, X₁₀, X₁₃, X₁₄, X₁₆ and X₁₇ is Gly (G) and the others are other than Gly (G).

103. (Previously presented) The pharmaceutical composition of Claim 94 comprising an ApoA-I agonist selected from the group consisting of:

peptide 1	PVLDLFRELLNELLEZLKQKLK	(SEQ ID NO:1)
peptide 2	GVLDLFRELLNELLEALKQKLKK	(SEQ ID NO:2)
peptide 3	PVLDLFRELLNELLEWLKQKLK	(SEQ ID NO:3)
peptide 4	PVLDLFRELLNELLEALKQKLK	(SEQ ID NO:4)
peptide 5	pVLDLFRELLNELLEALKQKLKK	(SEQ ID NO:5)
peptide 6	PVLDLFRELLNEXLEALKQKLK	(SEQ ID NO:6)
peptide 7	PVLDLFKELLNELLEALKQKLK	(SEQ ID NO:7)
peptide 8	PVLDLFRELLNEGLEALKQKLK	(SEQ ID NO:8)
peptide 9	PVLDLFRELGNELLEALKQKLK	(SEQ ID NO:9)
peptide 10	PVLDLFRELLNELLEAZKQKLK	(SEQ ID NO:10)
peptide 11	PVLDLFKELLQELLEALKQKLK	(SEQ ID NO:11)
peptide 12	PVLDLFRELLNELLEAGKQKLK	(SEQ ID NO:12)
peptide 13	GVLDLFRELLNEGLEALKQKLK	(SEQ ID NO:13)
peptide 14	PVLDLFRELLNELLEALOQOLO	(SEQ ID NO:14)
peptide 15	PVLDLFRELWNELLEALKQKLK	(SEQ ID NO:15)
peptide 16	PVLDLLRELLNELLEALKQKLK	(SEQ ID NO:16)
peptide 17	PVLELFKELLQELLEALKQKLK	(SEQ ID NO:17)

peptide 18	GVLDLDFRELLNELLEALKQKLK	(SEQ ID NO:18)
peptide 19	pVLDLDFRELLNEGLEALKQKLK	(SEQ ID NO:19)
peptide 20	PVLDLDFREGLNELLEALKQKLK	(SEQ ID NO:20)
peptide 21	pVLDLDFRELLNELLEALKQKLK	(SEQ ID NO:21)
peptide 22	PVLDLDFRELLNELLEGLKQKLK	(SEQ ID NO:22)
peptide 23	PLLELFKELLQELLEALKQKLK	(SEQ ID NO:23)
peptide 24	PVLDLDFRELLNELLEALQKKLK	(SEQ ID NO:24)
peptide 25	PVLDFFRELLNEXLEALKQKLK	(SEQ ID NO:25)
peptide 26	PVLDLDFRELLNELLELLKQKLK	(SEQ ID NO:26)
peptide 27	PVLDLDFRELLNELZEALKQKLK	(SEQ ID NO:27)
peptide 28	PVLDLDFRELLNELWEALKQKLK	(SEQ ID NO:28)
peptide 29	AVLDLDFRELLNELLEALKQKLK	(SEQ ID NO:29)
peptide 123	QVLDLDFRELLNELLEALKQKLK	(SEQ ID NO:123)
peptide 124	PVLDLFOELLNELLEALOQOLO	(SEQ ID NO:124)
peptide 125	NVLDLDFRELLNELLEALKQKLK	(SEQ ID NO:125)
peptide 126	PVLDLDFRELLNELGEALKQKLK	(SEQ ID NO:126)
peptide 127	PVLDLDFRELLNELLELLKQKLK	(SEQ ID NO:127)
peptide 128	PVLDLDFRELLNELLEFLKQKLK	(SEQ ID NO:128)
peptide 129	PVLELFNDLLRELLEALQKKLK	(SEQ ID NO:129)
peptide 130	PVLELFNDLLRELLEALKQKLK	(SEQ ID NO:130)
peptide 131	PVLELFKELLNELLDALRQKLK	(SEQ ID NO: 131)
peptide 132	PVLDLDFRELLNLEALQKKLK	(SEQ ID NO:132)
peptide 133	PVLELFERLLEDLLQALNKKLK	(SEQ ID NO:133)
peptide 134	PVLELFERLLEDLLKALNQKLK	(SEQ ID NO:134)
peptide 135	DVLDLDFRELLNELLEALKQKLK	(SEQ ID NO:135)
peptide 136	PALELFKDLLQELLEALKQKLK	(SEQ ID NO:136)
peptide 137	PVLDLDFRELLNEGLEAZKQKLK	(SEQ ID NO:137)
peptide 138	PVLDLDFRELLNEGLEWLKQKLK	(SEQ ID NO:138)
peptide 139	PVLDLDFRELWNEGLEALKQKLK	(SEQ ID NO:139)
peptide 140	PVLDLDFRELLNEGLEALOQOLO	(SEQ ID NO:140)
peptide 141	PVLDFFRELLNEGLEALKQKLK	(SEQ ID NO:141)
peptide 142	PVLELFRELLNEGLEALKQKLK	(SEQ ID NO:142)

and the N-terminal acylated and/or C-terminal amidated or esterified forms thereof, wherein X is Aib; Z is Nal; and O is Orn.

104. (Previously presented) The pharmaceutical composition of Claim 103 comprising an ApoA-I agonist that is SEQ ID NO: 4.

105. (Withdrawn) The pharmaceutical composition of Claim 94 comprising an ApoA-I agonist that is an altered form of formula (I).

106. (Withdrawn) The pharmaceutical composition of Claim 94 comprising an ApoA-I agonist wherein residues X₂, X₃, X₅, X₆, X₉, X₁₀, X₁₃, X₁₄, X₁₆, X₁₇ and X₂₁ are fixed according to formula I and at least one of residues X₁, X₄, X₇, X₈, X₁₁, X₁₂, X₁₅, X₁₈, X₁₉, X₂₀ and X₂₂ is conservatively substituted with another residue.

107. (Withdrawn) The pharmaceutical composition of Claim 105 comprising an ApoA-I agonist wherein:

X₁ is Pro (P), D-Pro (p), Gly (G) or Ala (A);

X₂ is Ala (A), Leu (L) or Val (V);

X₃ is Leu (L) or Phe (F);

X₅ is Leu (L) or Phe (F);

X₆ is Leu (L) or Phe (F);

X₉ is Leu (L) or Gly (G);

X₁₀ is Leu (L), Trp (W) or Gly (G);

X₁₃ is Leu (L), Gly (G) or Aib;

X₁₄ is Leu (L), Nal, Trp (W) or Gly (G);

X₁₆ is Ala (A), Nal, Trp (W), Gly (G), Leu (L) or Phe (F);

X₁₇ is Leu (L), Gly (G) or Nal;

X₂₁ is Leu (L); and

at least one of X₄, X₇, X₈, X₁₁, X₁₂, X₁₅, X₁₈, X₁₉, X₂₀, X₂₂ and X₂₃ is conservatively substituted with another residue.

108. (Withdrawn) The pharmaceutical composition of Claim 94 comprising an ApoA-I agonist wherein X₄, X₇, X₈, X₁₁, X₁₂, X₁₅, X₁₈, X₁₉ and X₂₂ are fixed according to formula I and

at least one of residues X₂, X₃, X₅, X₆, X₉, X₁₀, X₁₃, X₁₄, X₁₆, X₁₇, X₂₀ and X₂₁ is conservatively substituted with another residue.

109. (Withdrawn) The pharmaceutical composition of Claim 108 comprising an ApoA-I agonist wherein:

X₄ is Asp (D) or Glu (E);

X₇ is Lys (K), Arg (R) or Orn;

X₈ is Asp (D) or Glu (E);

X₁₁ is Asn (N) or Gln (Q);

X₁₂ is Glu (E) or Asp (D);

X₁₅ is Asp (D) or Glu (E);

X₁₈ is Gln (Q), Asn (N), Lys (K) or Orn;

X₁₉ is Gln (Q), Asn (N), Lys (K) or Orn;

X₂₀ is Lys (K) or Orn;

X₂₂ is Lys (K) or Orn;

X₂₃ is absent or Lys (K); and

at least one of X₁, X₂, X₃, X₅, X₆, X₉, X₁₀, X₁₃, X₁₄, X₁₆, X₁₇ and X₂₁ is conservatively substituted with another residue.

110. (Previously presented) The pharmaceutical composition of Claim 94 comprising an ApoA-I agonist wherein X₃ is Leu (L) or Phe (F), X₆ is Phe (F), X₉ is Leu (L) or Gly (G), and X₁₀ is Leu (L), Trp (W) or Gly (G).

111. (Withdrawn) The pharmaceutical composition of Claim 94 comprising an ApoA-I agonist wherein one helical turn is deleted.

112. (Withdrawn) The pharmaceutical composition of Claim 94 comprising an ApoA-I agonist wherein three, four, six, seven or eight residues X₁, X₂, X₃, X₄, X₅, X₆, X₇, X₈, X₉, X₁₀, X₁₁, X₁₂, X₁₃, X₁₄, X₁₅, X₁₆, X₁₇, X₁₈, X₁₉, X₂₀, X₂₁ and X₂₂ are deleted.

113. (Withdrawn) The pharmaceutical composition of Claim 112 comprising an ApoA-I agonist wherein 3 consecutive residues are deleted.

114. (Withdrawn) The pharmaceutical composition of Claim 112 comprising an ApoA-I agonist wherein 4 consecutive residues are deleted.
115. (Withdrawn) The pharmaceutical composition of Claim 112 comprising an ApoA-I agonist wherein two non-contiguous sets of 3 consecutive residues are deleted.
116. (Withdrawn) The pharmaceutical composition of Claim 112 comprising an ApoA-I agonist wherein two non-contiguous sets of 4 consecutive residues are deleted.
117. (Withdrawn) The pharmaceutical composition of Claim 112 comprising an ApoA-I agonist wherein one set of 3 consecutive residues and one set of 4 consecutive residues are deleted.
118. (Withdrawn) The pharmaceutical composition of Claim 112 comprising an ApoA-I agonist wherein 6, 7 or 8 consecutive residues are deleted.
119. (Withdrawn) A method of treating dyslipidemia in a subject in need of such treatment, said method comprising administering to the subject an effective amount of the pharmaceutical composition of Claim 63 or 86.
120. (Withdrawn) The method of Claim 119 wherein the dyslipidemia is atherosclerosis.
121. (Withdrawn) The method of Claim 119 wherein the dyslipidemia is cardiovascular disease.
122. (Withdrawn) The method of Claim 119 wherein said subject is human.
123. (Withdrawn) The method of Claim 119 wherein the pharmaceutical composition is administered intravenously.
124. (Withdrawn) The method of Claim 119 wherein the pharmaceutical composition is administered once weekly.

125. (Withdrawn) A method of treating septic shock in a subject in need of such treatment, said method comprising administering to the subject an effective amount of the pharmaceutical composition of Claim 63 or 86.

126. (Withdrawn) The method of Claim 125 wherein said subject is human.

127. (Withdrawn) The method of Claim 125 wherein the pharmaceutical composition is administered intravenously.